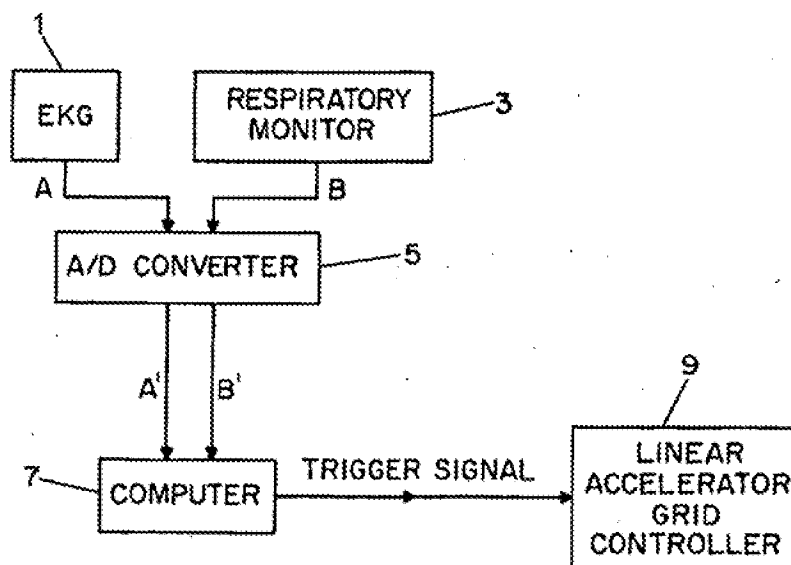




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(54) Title: APPARATUS AND METHOD TO GATE A SOURCE FOR RADIATION THERAPY



(57) Abstract

A radiation therapy apparatus and method for applying radiation to a patient in synchronism with one of a plurality of states of a cardiac cycle and one of a plurality of states of a respiratory cycle of the patient. An electrocardiograph (1) and a respiratory monitor (3) are operatively connected to the patient. A controller (7) is provided for receiving an output from said electrocardiograph indicative of which of said plurality of cardiac cycle states the cardiac cycle is presently in and for receiving an output from said respiratory monitor indicative of which of said plurality of respiratory cycle states the respiratory cycle is presently in. A radiation applicator (9) applies radiation to the patient in response to a trigger signal from the controller, said trigger signal being generated by said controller in response to said output from said electrocardiograph and said output from said respiratory monitor.

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APPARATUS AND METHOD TO GATE A SOURCE FOR RADIATION THERAPY5 BACKGROUND OF THE INVENTION

The present invention relates to an apparatus and a method to gate a source for radiation therapy. More particularly, the present invention relates to an apparatus and a method to gate
10 an x-ray source for radiation therapy. The radiation may be directed to target sites that move with or are affected by the cardiac and/or respiratory cycles. Such sites include, but are not limited to, the heart, the mediastinum, the lung, the breast, the kidney, the esophagus, the chest area, the liver, and the
15 peripheral blood vessels. Tumors at these listed sites, as well as other sites, may be treated.

Throughout this application various publications are referenced by Arabic numerals within parentheses. Full citations for these
20 references may be found at the end of the specification immediately preceding the claims. The disclosures of all of these publications in their entireties are hereby incorporated by reference into this application in order to more fully describe the state of the art to which this invention pertains.

25 Ionizing radiation delivered to coronary arteries before, during, and/or after balloon angioplasty has been shown to reduce the proliferation of smooth muscle cells and neointima formation, thereby inhibiting restenosis. (1-5) To date, most work in this
30 field has utilized temporary intraluminal insertion of high activity beta or gamma seed, wires, or fluids to deliver radiation. The treatment of restenosis is an important clinical problem in that 400,000 plus procedures are performed annually in the United States, at a total cost of approximately \$5
35 billion. The resulting restenosis rate is about 30-40%.

In any case, the insertion of radioactive sources into coronary arteries presents problems including radiation safety issues and possible excess exposure to patients and staff; possible

inhomogeneous dose distributions; and possible thrombus formation and/or embolization of the radioactive source in the arterial tree.

- 5 External beam irradiation has been proposed for the treatment of coronary arteries. (6-9) More generally, the application to a patient of such externally produced radiation and the problems associated therewith have been discussed. (10-25) In any case, conventional external beam radiation application suffers from the
- 10 disadvantage that coronary motion during treatment would necessitate the application of a radiation field of large size that would affect an unacceptably large volume of normal tissue surrounding the targeted treatment volume.
- 15 As an alternative, treatments could be fractionated to reduce normal tissue damage. However, such fractionation raises the additional complications of target localization and treatment reproducibility, as coronary arteries cannot be easily visualized on standard radiation oncology type simulation films or portal
- 20 images.

SUMMARY OF THE INVENTION

It is an object of the present invention to provide an apparatus and method in which the application of radiation from a linear accelerator or other radiation production source is synchronized with the occurrence of predetermined events in a patient's cardiac and respiratory cycles. This enables treatment with smaller field sizes and reduces normal tissue complications.

According to one aspect of the present invention, a radiation therapy apparatus for applying radiation to a patient in synchronism with one of a plurality of states of a cardiac cycle of a patient and one of a plurality of states of a respiratory cycle of a patient is provided, comprising an electrocardiograph operatively connected to the patient, a respiratory monitor operatively connected to the patient, control means for receiving an output from said electrocardiograph indicative of which of said plurality of cardiac cycle states the cardiac cycle is presently in and for receiving an output from said respiratory monitor indicative of which of said plurality of respiratory cycle states said respiratory cycle is presently in, and radiation application means for applying radiation to the patient in response to a trigger signal from said control means, said trigger signal being generated by said control means in response to said output from said electrocardiograph and said output from said respiratory monitor.

According to another aspect of the instant invention a radiation therapy apparatus for applying radiation to a patient in synchronism with one of a plurality of states of a cardiac cycle of a patient and one of a plurality of states of a respiratory cycle of a patient is provided, comprising an electrocardiograph operatively connected to the patient, a respiratory monitor operatively connected to the patient, display means for receiving an output from said electrocardiograph for displaying which of said plurality of cardiac cycle states the cardiac cycle was in at a given time and for receiving an output of said respiratory

monitor for displaying which of said plurality of respiratory cycle states said respiratory cycle was in at a given time, control means for receiving user input indicative of a selected point or interval of time when a chosen one of said plurality of cardiac cycle states overlaps with a chosen one of said plurality of respiratory states and for outputting a trigger signal at said selected point or interval of time based upon the output from the electrocardiograph input thereto and the output from the respiratory monitor input thereto, and radiation application means for applying radiation to the patient in response to the trigger signal from said control means.

According to another aspect of the instant invention a method of applying radiation to a patient in synchronism with one of a plurality of states of a cardiac cycle of a patient and one of a plurality of states of a respiratory cycle of a patient is provided, comprising operatively connecting an electrocardiograph to the patient, operatively connecting a respiratory monitor to the patient, receiving, at a control means, an output from said electrocardiograph indicative of which of said plurality of cardiac cycle states the cardiac cycle is presently in and for receiving, at the control means, an output from said respiratory monitor indicative of which of said plurality of respiratory cycle states said respiratory cycle is presently in, and applying radiation to the patient in response to a trigger signal from said control means, said trigger signal being generated by said control means in response to said output from said electrocardiograph and said output from said respiratory monitor.

According to another aspect of the instant invention a method of applying radiation to a patient in synchronism with one of a plurality of states of a cardiac cycle of a patient and one of a plurality of states of a respiratory cycle of a patient is provided, comprising operatively connecting an electrocardiograph to the patient, operatively connecting a respiratory monitor to the patient, displaying, on a display means, an output from said electrocardiograph indicative of which of said plurality of

cardiac cycle states the cardiac cycle was in at a given time, displaying, on the display means, an output from said respiratory monitor indicative of which of said plurality of respiratory cycle states said respiratory cycle was in at a given time, 5 receiving, at a control means, user input indicative of a selected point or interval of time when a chosen one of said plurality of cardiac cycle states overlaps with a chosen one of said plurality of respiratory cycle states, outputting a trigger signal from the control means at said selected point or interval 10 of time based upon the output from the electrocardiograph input to the control means and the output from the respiratory monitor input to the control means, and applying radiation to the patient in response to the trigger signal from said control means.

15 These and other advantages will become apparent from the detailed description, accompanying claims, and attached drawing figures.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 shows a block diagram of a first embodiment of the instant invention;

- 5 Fig. 2 shows a block diagram of a second embodiment of the instant invention;

Fig. 3 shows a block diagram of a third embodiment of the instant invention; and

10

Fig. 4 shows a block diagram of a fourth embodiment of the instant invention.

DETAILED DESCRIPTION OF THE DRAWINGS

According to one aspect of the present invention, a radiation therapy apparatus for applying radiation to a patient in synchronism with one of a plurality of states of a cardiac cycle of a patient and one of a plurality of states of a respiratory cycle of a patient is provided, comprising an electrocardiograph operatively connected to the patient, a respiratory monitor operatively connected to the patient, control means for receiving an output from said electrocardiograph indicative of which of said plurality of cardiac cycle states the cardiac cycle is presently in and for receiving an output from said respiratory monitor indicative of which of said plurality of respiratory cycle states said respiratory cycle is presently in, and radiation application means for applying radiation to the patient in response to a trigger signal from said control means, said trigger signal being generated by said control means in response to said output from said electrocardiograph and said output from said respiratory monitor.

The radiation application means may comprise an x-ray production means for applying x-ray radiation. The x-ray production means may include a linear accelerator. The device may further comprise a linear accelerator grid controller responsive to said trigger signal for controlling said linear accelerator.

The x-ray production means may include a rotating slit collimator. The device may further comprise a motor controller responsive to said trigger signal for controlling said rotating slit collimator.

The control means may comprise a computer. The device may further comprise an analog-to-digital converter connected to said electrocardiograph, said respiratory monitor, and said control means, said analog-to-digital converter being disposed between said electrocardiograph and said control means for converting an analog signal input thereto from the electrocardiograph into a

digital signal that is output to said control means and said analog-to-digital converter being disposed between said respiratory monitor and said control means for converting an analog signal input thereto from the respiratory monitor into a digital signal that is output to said control means.

The trigger signal from said control means may be produced in response to the detection by the control means of the occurrence within a predetermined time period of a predetermined one of said plurality of cardiac cycle states and a predetermined one of said plurality of respiratory states.

According to another aspect of the instant invention a radiation therapy apparatus for applying radiation to a patient in synchronism with one of a plurality of states of a cardiac cycle of a patient and one of a plurality of states of a respiratory cycle of a patient is provided, comprising an electrocardiograph operatively connected to the patient, a respiratory monitor operatively connected to the patient, display means for receiving an output from said electrocardiograph for displaying which of said plurality of cardiac cycle states the cardiac cycle was in at a given time and for receiving an output of said respiratory monitor for displaying which of said plurality of respiratory cycle states said respiratory cycle was in at a given time, control means for receiving user input indicative of a selected point or interval of time when a chosen one of said plurality of cardiac cycle states overlaps with a chosen one of said plurality of respiratory cycle states and for outputting a trigger signal at said selected point or interval of time based upon the output from the electrocardiograph input thereto and the output from the respiratory monitor input thereto, and radiation application means for applying radiation to the patient in response to the trigger signal from said control means.

The radiation application means may comprise an x-ray production means for applying x-ray radiation. The x-ray production means may include a linear accelerator. The device may further

comprise a linear accelerator grid controller responsive to said trigger signal for controlling said linear accelerator.

5 The x-ray production means may include a rotating slit collimator. The device may further comprise a motor controller responsive to said trigger signal for controlling said rotating slit collimator.

10 The control means may comprise a computer. The device may further comprise an analog-to-digital converter connected to said electrocardiograph, said respiratory monitor, and said control means, said analog-to-digital converter being disposed between said electrocardiograph and said control means for converting an analog signal input thereto from the electrocardiograph into a
15 digital signal that is output to said control means and said analog-to-digital converter being disposed between said respiratory monitor and said control means for converting an analog signal input thereto from the respiratory monitor into a digital signal that is output to said control means.

20 The control means may further comprise storage means for storing a plurality of selected points of time corresponding to a respective plurality of patients, whereby said control means outputs a trigger signal at one of said stored plurality of
25 selected points of time based upon the output from the electrocardiograph input thereto and the output from the respiratory monitor input thereto in response to user input selecting one of said plurality of patients.

30 According to another aspect of the instant invention a method of applying radiation to a patient in synchronism with one of a plurality of states of a cardiac cycle of a patient and one of a plurality of states of a respiratory cycle of a patient is provided, comprising operatively connecting an electrocardiograph
35 to the patient, operatively connecting a respiratory monitor to the patient, receiving, at a control means, an output from said electrocardiograph indicative of which of said plurality of

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cardiac cycle states the cardiac cycle is presently in, for receiving, at the control means, an output from said respiratory monitor indicative of which of said plurality of respiratory cycle states said respiratory cycle is presently in, and applying
5 radiation to the patient in response to a trigger signal from said control means, said trigger signal being generated by said control means in response to said output from said electrocardiograph and said output from said respiratory monitor.

10 According to another aspect of the instant invention a method of applying radiation to a patient in synchronism with one of a plurality of states of a cardiac cycle of a patient and one of a plurality of states of a respiratory cycle of a patient is provided, comprising operatively connecting an electrocardiograph
15 to the patient, operatively connecting a respiratory monitor to the patient, displaying, on a display means, an output from said electrocardiograph indicative of which of said plurality of cardiac cycle states the cardiac cycle was in at a given time, displaying, on the display means, an output from said respiratory
20 monitor indicative of which of said plurality of respiratory cycle states said respiratory cycle was in at a given time, receiving, at a control means, user input indicative of a selected point or interval of time when a chosen one of said plurality of cardiac cycle states overlaps with a chosen one of
25 said plurality of respiratory cycle states, outputting a trigger signal from the control means at said selected point or interval of time based upon the output from the electrocardiograph input to the control means and the output from the respiratory monitor input to the control means, and applying radiation to the patient
30 in response to the trigger signal from said control means.

Referring now to Fig. 1, a block diagram of a first embodiment of the instant invention is shown. As seen in this Fig., electrocardiograph 1, which is operatively connected to a patient
35 (not shown) to measure the patient's cardiac cycle, feeds an analog output signal A indicative of the cardiac cycle to analog-to-digital converter 5. Likewise, respiratory monitor 3, which

is operatively connected to the patient (not shown) to measure the patient's respiratory cycle, feeds an analog output signal B indicative of the respiratory cycle to the analog-to-digital converter 5.

5

The analog-to-digital converter 5 converts analog signal A into digital signal A' and provides the digital signal A' to computer 7. Analog-to-digital converter 5 likewise converts analog signal B into digital signal B' and provides the digital signal B' to
10 computer 7. Computer 7 generates a trigger signal at a point in time that a predetermined state of the cardiac cycle measured by the electrocardiograph 1 overlaps a predetermined state of the respiratory cycle measured by the respiratory monitor 3.

15 The trigger signal generated by the computer 7 is applied to linear accelerator grid controller 9 to cause a linear accelerator (not shown) that is connected to the linear accelerator grid controller 9 to irradiate the patient (not shown) at a predetermined position.

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Referring now to Fig. 2, in which the same reference numerals of Fig. 1 apply to the same elements and do not require a detailed explanation, a block diagram of a second embodiment of the instant invention is shown.

25

In this second embodiment of the instant invention the trigger signal output from computer 7 is provided to the motor controller of a rotating slit collimator to selectively irradiate the patient (not shown) at a predetermined position when the trigger
30 signal is received. Of course, the trigger signal could, in the alternative, be applied to a multi-leaf collimator, such as a rotating multi-leaf collimator.

35

Referring now to Fig. 3, in which the same reference numerals of Fig. 1 apply to the same elements and do not require a detailed explanation, a block diagram of a third embodiment of the instant invention is shown.

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In this third embodiment of the instant invention a display 22 displays a time-varying plot of the electrocardiograph output (signal a) and a time-varying plot of the respiratory monitor output (signal b). A user input device 20, such as a keyboard or mouse, for example, is operatively connected to computer 7.

A user may use the user input device 20 to select a chosen point in time when a chosen state of the cardiac cycle overlaps with a chosen state of the respiratory cycle, as indicated on the display 22. Computer 7 may include storage element 7a, such as a hard disk drive, floppy drive, or solid-state memory, for example. The storage element 7a may store, for each of a plurality of patients, data indicative of the chosen point in time when a chosen state of the cardiac cycle overlaps with a chosen state of the respiratory cycle.

Referring now to Fig. 4, in which the same reference numerals of Figs. 2 and 3 apply to the same elements and do not require a detailed explanation, a block diagram of a fourth embodiment of the instant invention is shown.

In this fourth embodiment of the instant invention the trigger signal output from computer 7 is provided to the motor controller of a rotating slit collimator to selectively irradiate the patient (not shown) at a predetermined position when the trigger signal is received.

The instant invention may utilize one or more megavoltage X-ray beams from a conventional linear accelerator or other source to provide a uniform dose coverage of 2-3 cm length of targeted arterial wall. Other sites that move during the cardiac and/or respiratory cycle to which radiation may be applied by the instant invention include, but are not limited to, the heart itself, the mediastinum, the lung, the breast, the kidney, the esophagus, the chest area, the liver, and the peripheral blood vessels. Tumors at these listed sites, as well as other sites, may be treated as may Hodgkins disease. The application of

radiation may be synchronized with the passive fill fraction of the cardiac cycle, where heart motion is minimal and arterial localization, for example, is reproducible. Further, radiation may be applied during a specific portion of the cardiac and/or respiratory cycles (for example, during the diastolic or systolic portion of the cardiac cycle) to a site such as a tumor that does not move substantially during the cycle but that is nevertheless affected by the cycle. It must be noted that the instant method and apparatus are useful for radiation therapy, in which application of radiation to the patient performs a therapeutic function, as opposed to diagnosis, in which radiation is applied to perform a diagnostic function.

Externally applied radiation treatments could be used for superficially located hemodialysis shunts. A single electron beam, which may be in the megavolt range, could be tailored to ideally match the desired treatment volume with rapid dose fall-off beyond the field edges and such radiation application may provide a more uniform dose distribution than an intraluminal insertion. Since the shunts are superficial, simple palpation could enable accurate field alignment, even for fractionated treatments.

Conventional fixed beam teletherapy may be utilized to apply the radiation to the patient. In the alternative, Intensity Modulated Radiation Therapy (IMRT) using Dynamic Multileaf Collimators (DMLC) may be used to apply the radiation to the patient.

In particular, IMRT entails rotation of the linear accelerator gantry in coordination with the opening and closing of the DMLC jaws. When delivering IMRT, at any desired combination of gantry angle and DMLC jaw position, the linear accelerator beams can be gated by the inventive method and apparatus to insure that radiation is only applied at the proper time.

It must be noted that although the present invention is described

by reference to particular embodiments thereof, many changes and modifications of the invention may become apparent to those skilled in the art without departing from the spirit and scope of the invention as set forth in the claims. For example, a
5 predetermined state or states of only a single one of the cardiac cycle or respiratory cycle may be utilized in the generation of the trigger signal. Further, other radiation producing sources besides those described may, of course, be utilized.

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What is claimed is:

1. A radiation therapy apparatus for applying radiation to
5 a patient in synchronism with one of a plurality of states of a
cardiac cycle of the patient and one of a plurality of states of
a respiratory cycle of the patient, comprising:

an electrocardiograph operatively connected to the patient;

a respiratory monitor operatively connected to the patient;

10 control means for receiving an output from said
electrocardiograph indicative of which of said plurality of
cardiac cycle states the cardiac cycle is presently in and for
receiving an output from said respiratory monitor indicative of
which of said plurality of respiratory cycle states said
15 respiratory cycle is presently in; and

radiation application means for applying radiation to the
patient in response to a trigger signal from said control means,
said trigger signal being generated by said control means in
response to said output from said electrocardiograph and said
20 output from said respiratory monitor.

2. The apparatus of claim 1, wherein said radiation
application means comprises an x-ray production means for
applying x-ray radiation.
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3. The apparatus of claim 2, wherein said x-ray production
means includes a linear accelerator.

4. The apparatus of claim 3, further comprising a linear
30 accelerator grid controller responsive to said trigger signal for
controlling said linear accelerator.

5. The apparatus of claim 2, wherein said x-ray production
means includes a rotating slit collimator.
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6. The apparatus of claim 5, further comprising a motor
controller responsive to said trigger signal for controlling said

rotating slit collimator.

7. The apparatus of claim 1, wherein said control means comprises a computer.

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8. The apparatus of claim 7, further comprising an analog-to-digital converter connected to said electrocardiograph, said respiratory monitor, and said control means, said analog-to-digital converter being disposed between said electrocardiograph and said control means for converting an analog signal input thereto from the electrocardiograph into a digital signal that is output to said control means and said analog-to-digital converter being disposed between said respiratory monitor and said control means for converting an analog signal input thereto from the respiratory monitor into a digital signal that is output to said control means.

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9. The apparatus of claim 1, wherein said trigger signal from said control means is produced in response to the detection by the control means of the occurrence within a predetermined time period of a predetermined one of said plurality of cardiac cycle states and a predetermined one of said plurality of respiratory cycle states.

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10. A radiation therapy apparatus for applying radiation to a patient in synchronism with one of a plurality of states of a cardiac cycle of the patient and one of a plurality of states of a respiratory cycle of the patient, comprising:

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an electrocardiograph operatively connected to the patient;
a respiratory monitor operatively connected to the patient;
display means for receiving an output from said electrocardiograph for displaying which of said plurality of cardiac cycle states the cardiac cycle was in at a given time and for receiving an output of said respiratory monitor for displaying which of said plurality of respiratory cycle states said respiratory cycle was in at a given time;

control means for receiving user input indicative of a

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selected point or interval of time when a chosen one of said plurality of cardiac cycle states overlaps with a chosen one of said plurality of respiratory cycle states and for outputting a trigger signal at said selected point or interval of time based upon the output from the electrocardiograph input thereto and the output from the respiratory monitor input thereto; and

radiation application means for applying radiation to the patient in response to the trigger signal from said control means.

11. The apparatus of claim 10, wherein said radiation application means comprises an x-ray production means for applying x-ray radiation.

12. The apparatus of claim 11, wherein said x-ray production means includes a linear accelerator.

13. The apparatus of claim 12, further comprising a linear accelerator grid controller responsive to said trigger signal for controlling said linear accelerator.

14. The apparatus of claim 11, wherein said x-ray production means includes a rotating slit collimator.

15. The apparatus of claim 14, further comprising a motor controller responsive to said trigger signal for controlling said rotating slit collimator.

16. The apparatus of claim 10, wherein said control means comprises a computer.

17. The apparatus of claim 16, further comprising an analog-to-digital converter connected to said electrocardiograph, said respiratory monitor, and said control means, said analog-to-digital converter being disposed between said electrocardiograph and said control means for converting an analog signal input thereto from the electrocardiograph into a digital signal that

is output to said control means and said analog-to-digital converter being disposed between said respiratory monitor and said control means for converting an analog signal input thereto from the respiratory monitor into a digital signal that is output to said control means.

18. The apparatus of claim 10, wherein said control means further comprises storage means for storing a plurality of selected points of time corresponding to a respective plurality of patients, whereby said control means outputs a trigger signal at one of said stored plurality of selected points of time based upon the output from the electrocardiograph input thereto and the output from the respiratory monitor input thereto in response to user input selecting one of said plurality of patients.

19. A method of applying radiation to a patient in synchronism with one of a plurality of states of a cardiac cycle of the patient and one of a plurality of states of a respiratory cycle of the patient, comprising:

operatively connecting an electrocardiograph to the patient;
operatively connecting a respiratory monitor to the patient;
receiving, at control means, an output from said electrocardiograph indicative of which of said plurality of cardiac cycle states the cardiac cycle is presently in and for receiving, at the control means, an output from said respiratory monitor indicative of which of said plurality of respiratory cycle states said respiratory cycle is presently in; and

applying radiation to the patient in response to a trigger signal from said control means, said trigger signal being generated by said control means in response to said output from said electrocardiograph and said output from said respiratory monitor.

20. A method of applying radiation to a patient in synchronism with one of a plurality of states of a cardiac cycle of the patient and one of a plurality of states of a respiratory cycle of the patient, comprising:

operatively connecting an electrocardiograph to the patient;
operatively connecting a respiratory monitor to the patient;
displaying, on display means, an output from said
electrocardiograph indicative of which of said plurality of
5 cardiac cycle states the cardiac cycle was in at a given time and
displaying, on the display means, an output from said respiratory
monitor indicative of which of said plurality of respiratory
cycle states said respiratory cycle was in at a given time;

receiving, at control means, user input indicative of a
10 selected point or interval of time when a chosen one of said
plurality of cardiac cycle states overlaps with a chosen one of
said plurality of respiratory cycle states and outputting a
trigger signal from the control means at said selected point or
interval of time based upon the output from the
15 electrocardiograph input to the control means and the output from
the respiratory monitor input to the control means; and

applying radiation to the patient in response to the trigger
signal from said control means.

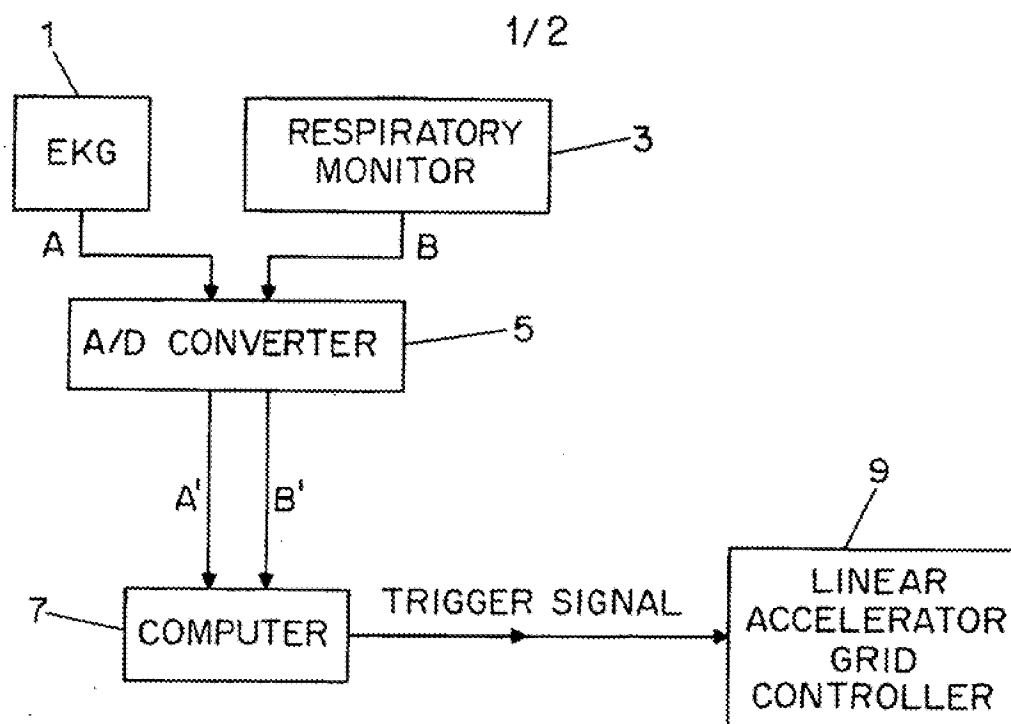


FIG. 1

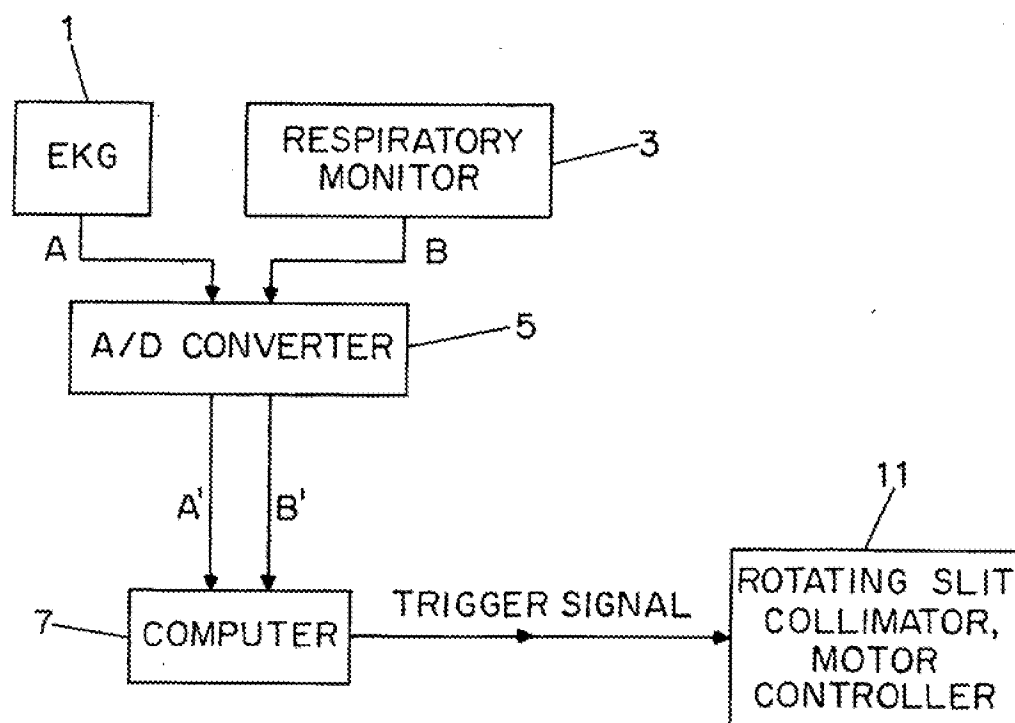


FIG. 2

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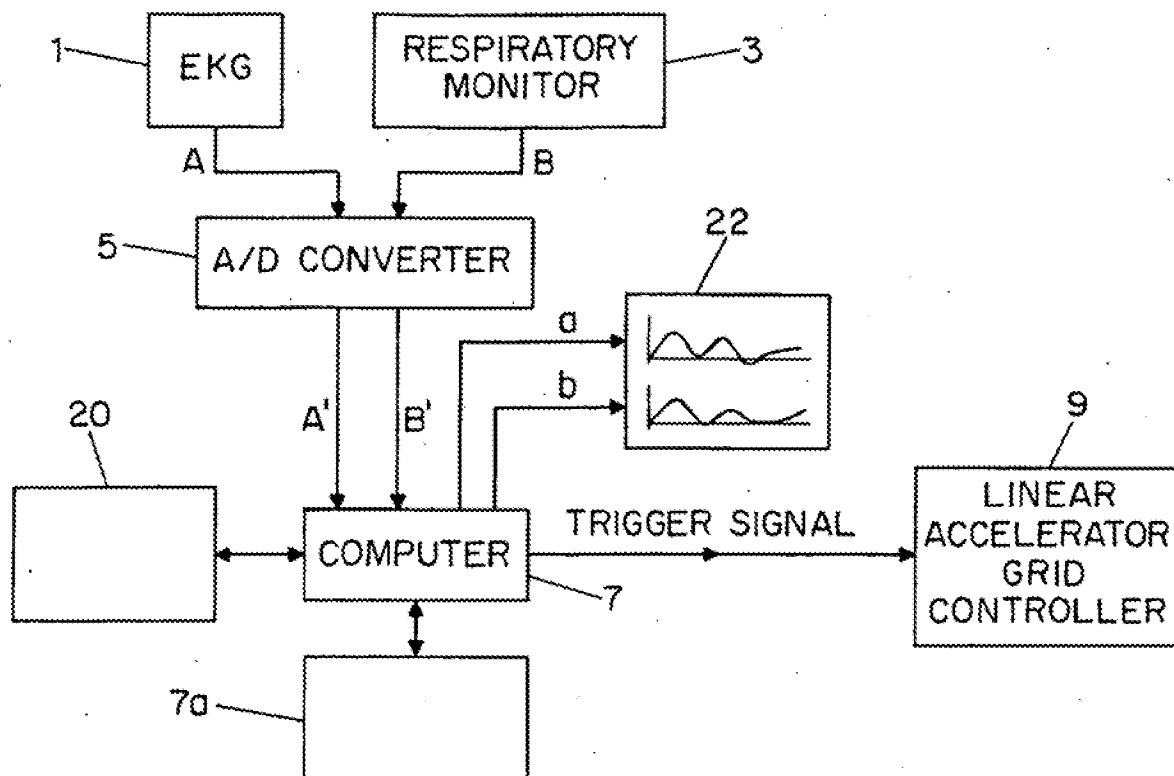


FIG. 3

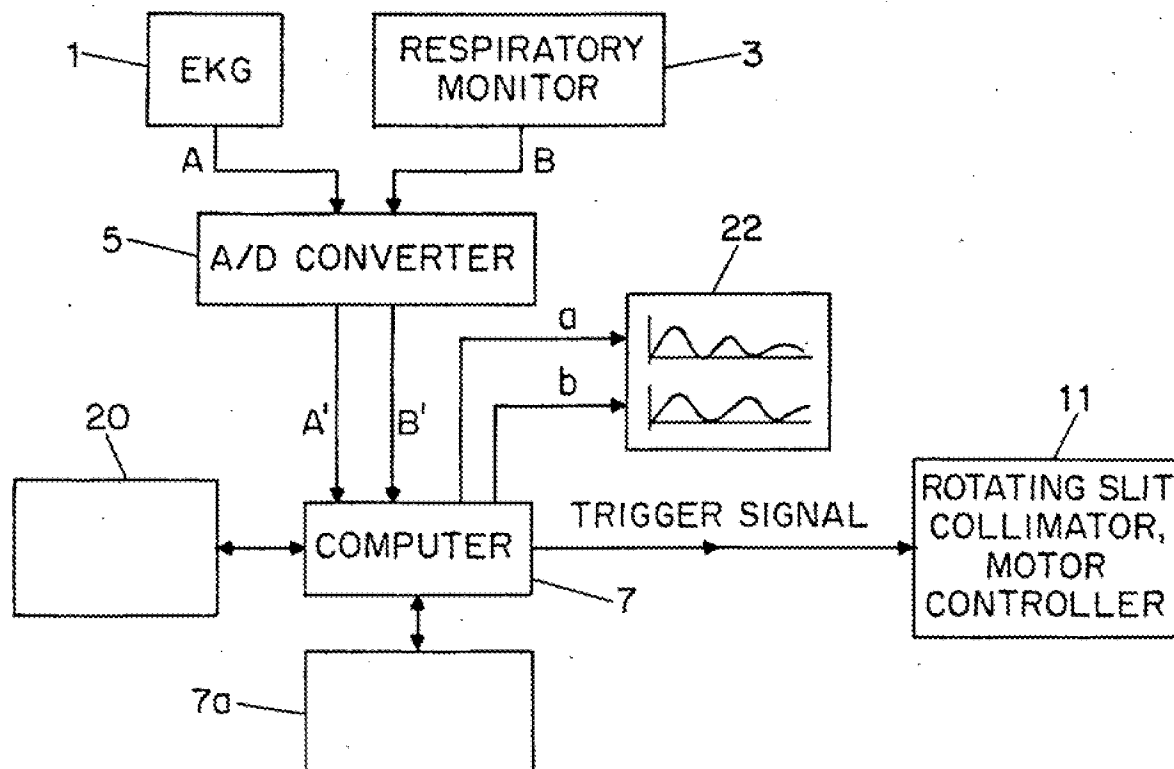


FIG. 4

INTERNATIONAL SEARCH REPORT

International application No. .
PCT/US97/18600

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : A61B 5/0205

US CL : 378/8, 95

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 378/8, 64, 65, 95

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 3,871,360 A (VAN HORN ET AL) 18 March 1975 (18.03.75) entire document.	1-20
A	US 4,031,884 A (HENZEL) 28 June 1977 (28.06.77).	
A	US 4,994,965 A (CRAWFORD ET AL) 19 February 1991 (19.02.91).	

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
A document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
E earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*A* document member of the same patent family
O document referring to an oral disclosure, use, exhibition or other means	
P document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

24 NOVEMBER 1997

Date of mailing of the international search report

04 DEC 1997

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